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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,143	11/03/2003	Robert M. Lorence	18029	3847

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EXAMINER	
KINSEY, NICOLE	
ART UNIT	**PAPER NUMBER**
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,143	LORENCE ET AL.	
	Examiner	Art Unit	
	Nicole E. Kinsey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-19 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/8/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Withdrawn Claim Rejections

The rejection of claims 1-23 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of applicants amendments to claims 1 and 9 and the cancellation of claim 23.

The rejection of claims 1-4, 6, 7 and 16-23 under 35 U.S.C. § 112, first paragraph, for lack of enablement, has been withdrawn in view of applicants' amendments to the claims and the cancellation of claim 23.

The rejection of claims 1-8, 13, 14 and 16-18 under 35 U.S.C. § 102(a) as being anticipated by Pecora et al. as evidenced by Laurie et al. has been withdrawn in view of applicants' amendment to claim 1. The references do not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

The rejection of claims 22 and 23 under 35 U.S.C. 102(a) as being anticipated by the 9th Annual Ottawa Life Sciences International Conference and Exhibition (November 4-6, 2002) has been withdrawn in view of applicants' cancellation of claims 22 and 23.

The rejection of claims 1-20 under 35 U.S.C. 102(b) as being anticipated by Roberts et al. (WO 00/62735) as evidenced by Chandler et al., Martensson et al., Drougas et al. and Wessels et al. has been withdrawn in view of applicants' amendment

to claim 1. The references do not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

The rejection of claims 1-8, 17 and 18 under 35 U.S.C. 102(b) as being anticipated by Lorence et al. (WO 94/25627) has been withdrawn in view of applicants' amendment to claim 1. The references do not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

The rejection of claims 1-4, 6, 17 and 18 under 35 U.S.C. 102(b) as being anticipated by Phuangsab et al. has been withdrawn in view of applicants' amendment to claim 1. The references do not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

The rejection of claims 1-4, 17 and 18 under 35 U.S.C. 102(b) as being anticipated by Reichard et al. has been withdrawn in view of applicants' amendment to claim 1. The references do not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

The rejection of claims 1-8, 17 and 18 under 35 U.S.C. 102(e) as being anticipated by Lorence et al. (US Patent No. 7,056,689) has been withdrawn in view of applicants' amendment to claim 1. The references do not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

The rejection of claims 9 and 10 under 35 U.S.C. 103(a) as being unpatentable over Pecora et al. has been withdrawn in view of applicants' amendment to claim 1. The combination of references does not teach or suggest treating a subject having a carcinoid tumor **and** carcinoid syndrome.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-19 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a carcinoid tumor with a replication-competent, oncolytic strain of Newcastle Disease Virus (NDV), does not reasonably provide enablement for any replication-competent strain of NDV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Scope of enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

Nature of the invention. The claims are drawn to a method of treating a carcinoid tumor and carcinoid syndrome by administering a replication-competent NDV to a mammal.

State of the prior art. At the time the invention was made, only certain NDV strains were labeled as "antineoplastic agents" for human tumors (See Sinkovics et al.). In addition, Sinkovics et al. states that "[v]arious NDV strains differ widely in their biological effects including oncolysis and without specific studies of a given NDV strain, generalizations that it is oncolytic just because it is a NDV strain are invalid and unacceptable." (See Sinkovics et al. entire article, especially page 11). Furthermore,

Wildner states, with respect to NDV, that "[s]train differences are substantial in respect to virulence, syncytium formation, replication, immune response, and oncolysis (See Wildner at pages 297-297, Newcastle disease virus heading). In addition, there are replication-competent, **non-oncolytic** strains of NDV (see Cassel et al., Cancer 1965, 18:863-868) where an oncolytic strain (73-T) of NDV was compared to a non-oncolytic strain (20Z) of NDV.

Breadth of the claims. The claims are extremely broad, encompassing treatment of a carcinoid tumor and carcinoid syndrome with any replication-competent NDV, even non-oncolytic strains of NDV.

Working examples. There are only working examples for the oncolytic, mesogenic strain MK107 of NDV.

Guidance in the specification. The specification teaches only the use of the oncolytic, mesogenic strain MK107 of NDV to treat a carcinoid tumor. There is no specific guidance regarding administering to a mammal any replication-competent non-oncolytic NDV strain.

Predictability of the art. The art with regard to NDV strains being oncolytic is acknowledged to be unpredictable as stated above under the heading *State of the prior art*. In the instant application, Applicants have not disclosed any non-oncolytic strains of NDV that can be utilized in accordance with the invention to treat a mammalian subject having a carcinoid tumor and carcinoid syndrome.

Amount of experimentation necessary. It is not known whether non-oncolytic strains of NDV would have any effect against a carcinoid tumor or carcinoid syndrome.

The claims must be commensurate in scope with the specification and one example is not enabling for the use of the class or genus of replication-competent NDVs. In ex parte Jackson, 217 USPQ 805, even a "description of several newly discovered strains of bacteria having one particularly desirable metabolic property in terms of conventionally measured culture characteristics and number of metabolic and physiological properties does not enable one of ordinary skill in the relevant art to independently discover additional strains having the same specific, desirable metabolic property". The results achieved in the examples are not predictive of the effect of any replication-competent strain of NDV on a carcinoid tumor and carcinoid syndrome as claimed.

Given the breadth of the claims, the lack of guidance in the specification, and the predictability of the art, it would require undue experimentation for one skilled in the art to use the claimed methods.

Response to Arguments

Applicants' arguments filed April 8, 2007 have been fully considered but they are not persuasive. Applicants argue that the literature supports the proposition that NDV generally is oncolytic and can be used in the claimed method. Applicants support this argument by citing Krishnamurthy et al. In Krishnamurthy et al., various strains of NDV were analyzed for, *inter alia*, growth on various tumor and non-tumor cell lines. Growth on selected tumor cell lines does not translate to oncolysis of tumor cells. There are strains of NDV that selectively grow on tumor cells versus non-tumor cells but do not

cause cell lysis. For example, NDV strain 20Z (discussed above) grows on tumor cells (not non-tumor cells) but is not oncolytic (see Cassel et al., page 867, first paragraph of Discussion). Further, other strains such as La Sota are also nonlytic. In a clinical trial (Newcastle Disease Virus (NDV) for Cancer Patients Resistant to Conventional Anti-Cancer Modalities, ClinicalTrials.gov Identifier: NCT00348842), both oncolytic and non-oncolytic strains of NDV were used. Thus, not every strain of NDV is oncolytic. How would applicants' claimed method work with a non-oncolytic strain of NDV such as 20Z?

Given the breadth of the claims, insufficient guidance in the specification, no working examples showing oncolysis with nonlytic strains of NDV, and the state of the art (see discussion above), it would require undue experimentation for one skilled in the art to practice the claimed methods.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-8 and 16-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 6, 7, 19, 22-25 and 27 of US Patent No. 7,056,689 ("the '698 patent"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating cancer in a mammal by administering a negative-stranded RNA virus (NDV). The '689 claims are drawn to treating a subject having a tumor with NDV. The '689 claims include treating a subject who may or may not have carcinoid syndrome (all that is required is that the subject has a tumor). Therefore, the scope of the '689 claims encompasses treating a subject with a carcinoid tumor and carcinoid syndrome.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 157-161, 163-170, 172, 174, 183, 196-219, and 230-232 of copending Application No. 09/958,809. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to infecting a tumor in a mammal with a virus comprising administering to said mammal an RNA virus, wherein said virus is administered as a first dose and one or more subsequent doses, and wherein the first dose is a desensitizing dose, to thereby infect said tumor (Treating a tumor in a mammal with an oncolytic virus will, at the same time, infect the tumor). The copending

claims are drawn to infecting a tumor with an interferon-sensitive, replication competent RNA virus. The copending claims include infecting a tumor in a subject who may or may not have carcinoid syndrome. Therefore, the scope of the copending claims encompasses infecting a tumor in a subject who has a carcinoid tumor and carcinoid syndrome.

Claims 1, 5-8, 13, 16, and 17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 6-8, 50, 51, 63-65, 69, 70, 73, 115-120, 132, 134, 136, and 144 of copending Application No. 10/167652 ("the '652 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating cancer by administering a replication competent, interferon sensitive clonal RNA virus to a mammal. The carcinoid tumor of the instant application is within the breadth of the term neoplasm, which is recited in the '652 application claims (see claims 7, 50 and 51). In addition, treating a neoplasm or tumor in a mammal with a virus will, at the same time, infect the neoplasm or tumor. Further, the copending claims include infecting a tumor in a subject who may or may not have carcinoid syndrome. Therefore, the scope of the copending claims encompasses infecting a tumor in a subject who has a carcinoid tumor and carcinoid syndrome.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 12, 17, 21,

22, 26-28 and 34 of copending Application No. 10/518,732 ("the '732 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to administering a therapeutic negative-stranded RNA virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially one or more desensitization doses of the virus followed by administering one or more escalated doses of the virus, wherein the amount of the virus in each of the one or more escalated doses is higher than the amount of virus in each of the desensitization doses. Although claims 13-15 of the instant application do not recite "the amount of the virus in the second and any subsequent desensitization dose is not less than the amount of the virus in the preceding desensitization dose," the scope of the '732 claims overlaps with claims 13-15 of the instant application.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/547,654 ("the '654 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to administering a therapeutic negative-stranded RNA virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially one or more desensitization doses of the virus followed by administering one or more escalated doses of the virus, wherein the amount of the virus in each escalated dose is higher than the amount of virus in each desensitization dose.

Although claims 13-15 of the instant application do not recite a time period between the desensitizing dose and the escalated dose or a rate for administration, the scope of the '654 claims overlaps with claims 13-15 of the instant application.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/548,057 ("the '057 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to administering a therapeutic negative-stranded RNA virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially one or more desensitization/initial doses of the virus followed by administering one or more escalated/subsequent doses of the virus, wherein the amount of the virus in each escalated dose is higher than the amount of virus in each desensitization dose.

Claims 1, 5-8 and 16-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14, 17, 18, 21, 22, 33, 34, 36-39, and 41 of copending Application No. 11/441,201. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating cancer or a tumor by administering to a mammal a negative-stranded RNA virus. The copending claims are drawn to treating a subject having a tumor with NDV. The copending claims

include infecting a tumor in a subject who may or may not have carcinoid syndrome. Therefore, the scope of the copending claims encompasses infecting a tumor in a subject who has a carcinoid tumor and carcinoid syndrome.

Applicants' argument regarding the double patenting rejections above is acknowledged but is not persuasive for the reasons above.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole E. Kinsey, Ph.D.
Examiner
Art Unit 1648

/nk/

/Stacy B. Chen/ 6-14-2007
Primary Examiner, TC1600